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Bacteremia in Lung Transplant Recipients in the Current Era

S. Husain[a,*], K. M Chan[b], S. M. Palmer[c], D. Hadjiliadis[d], A. Humar[e], K. R McCurry[f], M. M. Wagener[a] and N. Singh[a]

[a] *Division of Infectious Diseases, University of Pittsburgh, Pittsburgh, Pennsylvania, USA*
[b] *Division of Pulmonary and Critical Care, University of Michigan Medical Center, Ann Arbor, Michigan, USA*
[c] *Division of Pulmonary and Critical Care, Duke University Medical Center, Durham, North Carolina, USA*
[d] *Division of Pulmonary and Critical Care, University of Pennsylvania, Philadelphia, Pennsylvania, USA*
[e] *Transplantation Infectious Diseases, University Health Network, Toronto General Hospital, Toronto, Ontario, Canada*
[f] *Division of Surgery,University of Pittsburgh, Pittsburgh, Pennsylvania, USA*
[*] *Corresponding author: Shahid Husain, husains@dom.pitt.edu*

Current trends in the epidemiology, outcome and variables influencing mortality in bacteremic lung transplant recipients have not been fully described. We prospectively studied bacteremias in lung transplant recipients in a multicenter study between 2000–2004. Bacteremia was documented in 56 lung transplant recipients, an average of 172 days after transplantation. Multiple antibiotic resistance was documented in 48% of the isolates; these included 57% of the Gram-negative and 38% of the Gram-positive bacteria. Pulmonary infection was the most common source of resistant gram-negative bacteremias. Mortality rate at 28 days after the onset of bacteremia was 25% (14/56). Mechanical ventilation and abnormal mental status correlated independently with higher mortality ($p < 0.05$ for both variables). Bacteremia remains a significant complication in lung transplant recipients and is associated with considerable mortality. Recognition of variables portending a high risk for antibiotic resistance and for poor outcome has implications relevant for optimizing antibiotic prescription and for improving outcomes in lung transplant recipients.

Key words: Bacteremia, bacterial infections, lung transplants

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Introduction

The unique susceptibility of lung transplant recipients to infectious complications is well recognized. Infections are also a significant contributor to poor outcome, accounting for 25–37% of the post-transplant deaths in these patients (1–3). Bacteremias are an important infection in organ transplant recipients (4,5). In comparison to other major infections however, e.g. fungal and viral infections, there is striking paucity of systematically conducted studies on bacteremias in lung transplant recipients (1,6). In a study in adult lung transplant recipients conducted between 1992–98, the overall incidence of bacteremia was 25% and staphylococci were the most common etiologic agents (1).

Immunosuppressive regimens, patient characteristics and antimicrobial prescription practices have continued to evolve and are likely to have an impact on infectious complications after lung transplantation (7,8). The goals of this study were to determine the spectrum of bacteremias, assess risk factors for bacteremia due to antibiotic-resistant bacteria and determine the outcome in bacteremic lung transplant recipients.

Methods

The study population comprised prospectively identified lung transplant recipients with bacteremia at our institutions between July 2000 and February 2004. Institutional review board approval was obtained as per local requirements. Immunosuppression and antimicrobial prophylaxis was administered according to the standard practice at each institution. Immunosuppressive regimen was tacrolimus based at one and cyclosporine based at the other sites. Two of the study sites utilized T-cell induction with IL-2 receptor antibodies or rabbit antithymocyte globulin. Antimicrobial prophylaxis employed at the participating sites is outlined in Table 1.

Definitions

Definition of bacteremia and determination of its source was based on the criteria proposed by the Centers for Disease Control and Prevention and as previously reported in transplant recipients (9,10). Isolation of bacteria from a single blood culture in the presence of clinical symptoms or signs of infection was considered true bacteremia (9). Bacteremia caused by common skin contaminants was considered significant only if the organism was isolated from ≥ 2 blood cultures and clinical manifestations of infection were present (9). Bacteremia was considered primary if the offending pathogen was not related to infection at another site or if it was vascular-catheter related (9). The source was considered pulmonary if the same bacteria was also isolated from the pleural fluid or

Table 1: Antimicrobial prophylaxis employed at the participating sites

Institution	Antimicrobial prophylaxis
Toronto General Hospital	Cefuroxime for 48 h unless cystic fibrosis was present, in which case the perioperative antibiotics were based on the colonizing organisms and continued for 2 weeks. Patients with cystic fibrosis also received inhaled tobramycin.
Henry Ford Hospital	Vancomycin plus ceftazidime or cipro-floxacin for 7 days. In patients with cystic fibrosis, antibiotics were adjusted based on perioperative cultures.
Duke University	Vancomycin plus ceftazidime for 7–10 days. Antibiotics were modified based on donor bronchial washing isolates and perioperative cultures in cystic fibrosis patients. Inhaled colistin and tobramycin were also employed for 3 months in patients with cystic fibrosis.
University of Pittsburgh	Ceftazolin plus aztreonam for 48 h. Antibiotic selection was based on perioperative cultures in patients with cystic fibrosis.

respiratory tract cultures, including bronchoalveolar lavage in the presence of clinical signs and symptoms of pneumonia (9).

Multiple-antibiotic resistance was defined as enterococci resistant to vancomycin; *S. aureus* resistant to methicillin; enterobacteriaceae resistant to at least two of the following: extended spectrum penicillins, quinolones, third-generation cephalosporins, or aminoglycosides; and *P. aeruginosa* or other nonfermenting Gram-negative bacteria resistant to at least two of the following: extended spectrum penicillins, quinolones, generation cephalosporins, aztreonam, carbapenems, or aminoglycosides (11,12). Prior antibiotic use was defined as use of antibiotics for $\geq$ 1 day within 14 days preceding the onset of bacteremia. Discordant antibiotic therapy was defined as receipt for the first 2 days (after the blood culture was obtained) of an antibiotic agent or regimen that was inactive *in vitro* against the bacteria subsequently isolated in the blood culture (13). T-cell antibodies were classified as nondepleting (IL-2 receptor antibodies such as basiliximab or dacluzimab) or depleting (antithymocyte globulin) depending upon whether they reduce responsiveness of T-cells with or without depleting them (14).

Statistical analysis

Statistical analysis was conducted using STATA (Intercooled Stata 7.0, College Station, TX). Categorical data were compared using the Fisher exact test. The Mann-Whitney test was used to compare continuous data and was constructed to examine the effects of multiple risk factors on outcome. Factors significant at the level of 0.05 or lower by univariate analysis were analyzed in a logistic regression model and considered to be significant if p-value was $\leq$ 0.05.

Results

Bacteremia was documented in 56 lung transplant recipients. These included 35 of 305 patients who underwent lung transplantation during the study period, yielding an incidence rate of 11.5%. The clinical and demographic characteristics of the patients are outlined in Table 2. Pulmonary (46%, 26/56) and vascular catheter infections (41%, 23/56) accounted for a majority of the episodes of bacteremia; the latter included 14 long-term access (dialysis or implantable catheters) and 9 short-term (or central venous catheters). In all, 52% (29/56) of the bacteremias were due to Gram-negative and 46% (26/56) due to Gram-positive bacteria; one patient had bacteremia due to both *P. aeruginosa* and MRSA (Table 3). *Pseudomonas aeruginosa* (23%, 13/56*), Burkholderia cepacia* (9%, 5/56) and *Klebsiella pneumoniae* (7%, 4/56) were the most commonly documented Gram-negative bacteria. These bacteria accounted for 67% of all episodes of bacteremia resulting from a pulmonary source. *S. aureus* was the predominant Gram-positive pathogen associated with bacteremias. Vascular catheters followed by pulmonary infection were the most frequently documented sources of S. *aureus* bacteremia (Table 3).

Table 2: Demographic and clinical characteristics of the study patients

Number of patients	56
Age, median (range)	54 (18 to 67 years)
Gender	
Female	42.9% (24/56)
Male	57.1% (32/56)
Race	
Caucasian	89.3% (50/56)
African American	7.1% (4/56)
Hispanic	1.8% (1/56)
Unknown	1.8% (1/56)
Type of transplant	
Bilateral	53.6% (30/56)
Single	41.1% (23/56)
Heart-lung	5.4% (3/56)
Underlying lung disease	
Chronic obstructive pulmonary disease	42.9% (24/56)
Cystic fibrosis	19.6% (11/56)
Sarcoidosis	12.5% (7/56)
Pulmonary fibrosis	8.9% (5/56)
Alpha-1 antitrypsin deficiency	5.3% (3/56)
Primary pulmonary hypertension	3.6% (2/56)
Other	7.1% (4/56)
Immunosupression	
Tacrolimus	76.8% (43/56)
Cyclosporine A	19.6% (11/56)
Azathioprine	44.6% (25/56)
Mycophenolate mofetil	33.9% (19/56)
Sirolimus	5.3% (3/56)
Prednisone	21.4% (12/56)
T-cell antibody induction	37.5% (21/56)
Diabetes mellitus	35.7% (20/56)
Renal failure*	23.2% (13/56)
Dialysis	19.6% (11/56)

*Defined as creatinine $>$ 2.0 mg/dL.
Other includes silicosis 1, rheumatoid lung 1, eosinophilic lung disease 1 and bronchiolitis obliterans 1.

Table 3: Pathogens associated with bacteremia stratified by the source

	Source of the bacteremia					
Bacteria	Pulmonary	Vascular catheter	Surgical site	Urinary tract	Abdominal	Total
Gram-negative						
Glucose nonfermenters						
Pseudomonas aeruginosa	8	4	-	-	-	12
Burkholderia cepacia	4	-	1	-	-	5
Acinetobacter baumanii	1	-	-	-	-	1
Stenotrophomonas maltophilia	-	1	-	-	-	1
Pandoraea pnomenosa	1	-	-	-	-	1
Glucose fermenters						
Klebsiella pneumoniae	3	-	-	-	1	4
Serratia marcesens	-	2	-	-	-	2
Proteus mirabilis	-	1	-	-	-	1
Pantoea agglomerans	1	-	-	-	-	1
Gram-positive						
MRSA*	2	3	1	-	-	6
MSSA**	1	1	-	-	-	2
VRE†	1	1	-	-	1	3
Enterococcus fecalis	-	4	-	-	1	5
Staphylococcus epidermidis	1	3	-	-	-	4
Staphylococcus hominis	-	1	-	-	-	1
Viridans streptococci	1	-	-	-	-	1
Streptococcus pneumoniae	1	-	-	-	-	1
Clostridium spp.	-	-	-	-	1	1
Corynebacterium spp.	-	1	-	-	-	1
Polymicrobial						
P. aeruginsosa + P mirabilis	-	-	-	1	-	1
P. aeruginosa + MRSA	1	-	-	-	-	1
E. fecalis + S. epidermidis	-	1	-	-	-	1
Total	26	23	2	1	4	56

*MRSA = methicillin-resistant *S. aureus*.
** MSSA = methicillin-sensitive *S. aureus*.
†VRE = vancomycin-resistant *Enterococcus faecium*.

Enterococci were the second most commonly occurring Gram-positive etiologic agents for bacteremia (Table 3).

Time to onset

The median time to onset of bacteremia after transplantation was 172 days (interquartile range 45–423 days). In all, 20% of the bacteremias occurred within 30 days, 18.2% between 30–90 days, 34.5% between 91 days–1 year and 27.3% >1 year posttransplantation. Pulmonary infection was the most frequently documented source of bacteremia up to one year after transplantation; 54.5% of the bacteremias within 30 days, 40% between 31-90 days and 52.6% between 91 days—1 year posttransplant were of pulmonary origin. After 1 year, the leading portal of entry was vascular catheters (53.3%) whereas pulmonary infections accounted for 26.7% of the bacteremias during this period. Only 7% (1/14) of the catheter-related infections within 1 year compared to 50% (4/8) after 1 year posttransplant were due to dialysis catheters.

Since bacteremias occurring within 30 days of transplantation may be amenable to antimicrobial prophylaxis, we analyzed variables associated with early (within 30 days posttransplant) versus late-onset bacteremia (after 30 days). Patients with early onset bacteremias were significantly more likely to still be intubated at 30 days and to have received T-cell depleting antibody induction (Table 4). Other clinically relevant variables did not differ for the two groups (Table 4).

Bacteremia due to multiple antibiotic-resistant bacteria

Multiple antibiotic resistance was documented in 48% (27/56) of the isolates. A total of 57% (17/30) of the Gram-negative bacteremias were due to multiply-antibiotic resistant bacteria; these included 50% of the *Pseudomonas aeruginosa*, 100% of the *Burkholderia cepacia* and 50% of the *Klebsiella pneumoniae* isolates. Pulmonary infection was the most common source of resistant Gram-negative bacteremias (71%, 12/17). In all, 35% (6/17) of the patients with cystic fibrosis compared to 8% (1/13) with other underlying lung diseases had resistant Gram-negative bacteremia ($p = 0.10$) (Table 5). When patients with *B. cepacia* were excluded, the proportion of patients with cystic fibrosis who had bacteremia due to multiple antibiotic-resistant Gram-negative bacteria was similar to noncystic fibrosis patients (50%, 1/2 vs. 48%, 11/23, $p = 0.99$).

Table 4: Variables associated with bacteremia occurring within 30 days (early-onset) versus after 30 days posttransplant (late onset)

Variable	Bacteremias within 30 days posttransplant (n = 11)	Bacteremia after 30 days posttransplant (n = 45)	p Value
Univariate analysis			
Age, median	52	54	0.27
Type of transplant			
Bilateral	63% (7/11)	51% (23/45)	0.51
Underlying lung disease			
Cystic fibrosis	27% (3/11)	18% (8/45)	0.67
Chronic obstructive pulmonary disease	36% (4/11)	42% (19/45)	0.99
Mechanical ventilation	82% (9/11)	27% (13/45)	0.002
Source of bacteremia			
Pulmonary	54% (6/11)	42% (19/45)	0.51
Vascular-catheter	36% (4/11)	44% (20/45)	0.74
Antibiotic-resistant bacteria	45% (5/11)	49% (22/45)	0.99
Nonfermenter gram-negative bacteria	36% (4/11)	31% (14/45)	0.73
T-cell antibody use	67% (7/11)	31% (14/45)	0.051
Depleting T-cell antibody use	36% (4/11)	7% (3/45)	0.022
Multivariate analysis	Odds ratio	95% CI	
Mechanical ventilation	11.59	1.94 – 69.28	0.007
T-cell depleting antibody	8.66	1.13 – 66.10	0.03

Table 5: Factors associated with bacteremia due to multiple antibiotic-resistant versus sensitive Gram-negative bacteria

Factor	Resistant (n = 17)	Sensitive (n = 13)	Significance level
Age, median (years)	52.5	55	0.15
Type of transplant			
Bilateral	71% (12/17)	46% (6/12)	0.18
Single	29% (5/17)	46% (6/12)	
Heart-lung	0	8%(1/13)	
Underlying lung disease			
Cystic fibrosis	35% (6/17)	8% (1/13)	0.10
COPD*	35% (6/17)	54% (7/13)	0.46
Alpha-1 antitrypsin deficiency	12% (2/17)	0/13	0.49
Sarcoidosis	12% (2/17)	8% (1/13)	0.99
Pulmonary fibrosis	6% (1/17)	15% (2/13)	0.56
Primary pulmonary hypertension	0/17	8% (1/13)	0.43
Other	0/17	8% (1/13)	0.43
Immunosuppression			
Primary			
Tacrolimus	82% (14/17)	69% (9/13)	0.66
Cyclosporine A	18% (3/17)	31% (4/13)	
Mycophenolate mofetil	41% (7/17)	23% (3/13)	0.44
T-cell antibodies	29% (5/17)	31% (4/13)	0.99
Diabetes mellitus	47% (8/17)	31% (4/13)	0.46
Prior antibiotic use	65% (11/17)	23% (3/13)	0.03
Renal failure at baseline	18% (3/17)	15% (2/13)	0.99
Mechanical ventilation	53% (9/17)	15% (2/13)	0.06
Source			
Pulmonary	71% (12/17)	46% (6/13)	0.26
Urinary tract	6% (1/17)	8% (1/13)	0.99
Vascular catheter	12% (2/17)	38% (5/13)	0.19
Intraabdominal	6% (1/17)	8% (1/13)	0.99

*COPD = chronic obstructive pulmonary disease.

When variables associated with multiple antibiotic-resistant versus sensitive Gram-negative bacteria were analyzed, only prior antibiotic use correlated significantly with antibiotic resistance (65%, 11/17 versus 23%, 3/13, p = 0.03) (Table 5). Of Gram-positive bacteria, 38% (10/26) were multiple antibiotic-resistant; these included six *S. aureus* and four enterococcal isolates. The only variable significantly associated with resistant Gram-positive

Table 6: Risk factors for bacteremia due to multiple antibiotic-resistant versus sensitive Gram-positive bacteria

Factor	Resistant (n = 10)	Sensitive (n = 16)	Significance level
Age, median, years	49	53	0.48
Prior antibiotics	70% (7/10)	62.5% (10/16)	0.99
Type of transplant			0.42
Bilateral	60% (6/10)	37% (6/16)	
Unilateral	30% (3/10)	56% (9/16)	
Heart-lung	10% (1/10)	6% (1/16)	
Underlying disease			
Cystic fibrosis	20% (2/10)	12% (2/16)	0.63
COPD*	40% (4/10)	37% (6/16)	0.99
Alpha-1 antitrypsin deficiency	0/10	6% (1/16)	0.99
Sarcoidosis	20% (2/10)	12% (2/16)	0.63
Pulmonary fibrosis	10% (1/10)	6% (1/16)	0.99
Primary pulmonary hypertension	0/10	16%(1/16)	0.99
Other	10%(1/10)	19% (3/16)	0.99
Immunosuppression			
Primary			
Tacrolimus	70% (7/10)	81% (13/16)	0.64
Cyclosporine A	30% (3/10)	19% (3/16)	
Mycophenolate mofetil	70% (7/10)	12% (2/16)	0.008
T-cell antibodies	60% (6/10)	37% (6/16)	0.42
Diabetes mellitus	30% (3/10)	31% (5/16)	0.99
Renal failure	20% (2/10)	25% (4/16)	0.99
Mechanical ventilation	60% (6/10)	44% (7/16)	0.69
Source			
Pulmonary	20% (2/10)	25% (4/16)	0.99
Vascular catheter	60% (6/10)	62% (10/16)	0.99
Intraabdominal	0/10	12% (2/16)	0.51
Surgical site	20% (2/10)	0% (0/16)	0.14

*COPD = chronic obstructive pulmonary disease.

bacteremias was the receipt of mycophenolate mofetil (Table 6); resistant Gram-positive bacteremias in 5/7 mycophenolate mofetil recipients were due to MRSA.

Discordant initial antibiotic use

Twenty-one percent (12/56) of the bacteremic patients received discordant antibiotics; these included 23.3% (7/30) of those with Gram-negative and 19.2% (5/26) of those with Gram-positive bacteremias. Receipt of discordant antibiotics was documented in 28% (7/25) of the patients with a pulmonary portal and in 9.1% (2/22) of those with vascular catheters as the source of bacteremias. Patients with cystic fibrosis received discordant antibiotics in 27.3% (3/11) and those with COPD in 13% (3/23) of the cases. The aforementioned differences, however, were not statistically significant.

Mortality

Overall mortality rate at 28 days in the patients with bacteremia was 25% (14/56). Mortality rate was 33% for patients with *Pseudomonas aeruginosa*, 20% for *Burkholderia cepacia*, 17% for MRSA and 25% for those with enterococcal bacteremia. When stratified by time elapsed since transplantation, mortality was 36.4% (4/11) for bacteremias occurring within 30 days, 30% (3/10) between 31–90 days, 26.3% (5/19) between 91 days–1 year and 20% (3/15) for bacteremias occurring >1 year posttransplantation. In univariate analysis, abnormal mental status, mechanical ventilation, Gram-negative bacteremia and multiple antibiotic resistance were significantly associated with mortality (Table 7). In a logistic regression model that included the aforementioned variables, mechanical ventilation and abnormal mental status independently correlated with higher mortality (Table 7).

Discussion

Several observations based on our study are clinically relevant with regards to bacteremia in lung transplant recipients. Thoracic organ transplant recipients are uniquely susceptible to pulmonary complications (15). Our data show that 50% of the bacteremias in the first posttransplant year were of pulmonary origin. After 1 year, the proportion of bacteremias that were due to pulmonary infections declined to 26.7% and vascular catheters emerged as the leading source of bacteremia (53.3%). In lung transplant recipients receiving calcineurin-inhibitor agents, renal failure is an increasingly recognized morbidity. Deterioration in renal function typically ensues early (16,17), with 91% of the patients experiencing renal dysfunction by 6 months (16) and 5–8% ultimately requiring hemodialysis (17,18). We note that one-half of the vascular catheter associated

Table 7: Factors associated with mortality at 28 days in the study patients (univariate analysis)

Factor	Died (n = 14)	Lived (n = 42)	Significance level
Univariate analysis			
Age, median, years	50	49	0.58
Type of lung transplant			
Bilateral	57.1% (8/14)	52.9% (22/42)	0.89
Unilateral	42.9% (6/14)	40.5% (17/42)	
Heart-lung	0/16	7.1%(3/42)	
Underlying disease			
Cystic fibrosis	7.1% (1/14)	23.8%(10/42)	0.26
Chronic obstructive pulmonarydisease	57.1% (8/14)	35.7% (15/42)	0.21
Alpha-1 antitrypsin deficiency	14.3% (2/14)	2.4% (1/42)	0.15
Sarcoidosis	19% (2/14)	11.9% (5/42)	0.99
Pulmonary fibrosis	0/14	9.5% (4/42)	0.56
Primary pulmonary hypertension	0/14	11.9% (5/42)	0.32
Silicosis	6% (1/14)	0/42	0.25
Rheumatoid lung	0/14	2.4% (1/42)	0.99
Other	6%(1/14)	9.5% (4/42)	0.99
Immunosuprression			
Primary			
Tacrolimus	92.9% (13/14)	71.4% (30/42)	0.15
Cyclosporine A	7.1% (1/14)	28.6% (12/42)	
Mycophenolate mofetil	50% (7/14)	28.6% (12/42)	0.19
T-cell antibodies	42.9% (6/14)	35.7% (15/42)	0.75
Diabetes mellitus	21.4% (3/14)	40.5% (17.42)	0.33
Renal failure	28.6% (4/14)	16.7% (7/42)	0.43
Signs & symptoms*			
Fever	64.3%(9/14)	76.2% (32/42)	0.48
Hypothermia	14.3% (2/14)	4.8% (2/42)	0.25
Abnormal mental status	78.6% (11/14)	4.8% (2/42)	<.0001
Mechanical ventilation	100% (14/14)	35.7% (15/42)	<.0001
Gram-negative bacteria	78.6% (11/14)	45.2% (19/21)	0.03
Multiple antibiotic-resistant bacteria	78.6% (11/14)	38.1% (16/42)	0.01
Discordant antibiotic use	42.8% (6/14)	14.2% (6/42)	0.05
Multivariate analysis	Odds ratio	95% CI	
Gram negative bacteremia	10.8	0.87 – 133.83	0.063
Mechanical ventilation**	–	–	< 0.0001
Abnormal mental status	21.95	1.88 – 255.86	0.014
Multiple antibiotic resistance	5.17	0.51 – 51.95	0.162

*Fever was defined as temperature of 100°F or greater and hypothermia as temperature equal to or less than 95°F (10).
**The odds ratio and confidence intervals for mechanical ventilation could not be calculated as all patients with mechanical ventilation died yielding an odds ratio that approached infinity because of zero value.

bacteremias after the first posttransplant year in our study were dialysis catheter-related.

Assessment of trends in the epidemiology of bacterial infections in immunosup-pressed hosts have often focused on bloodstream infections as a benchmark (11,15,19). In liver and heart transplant recipients, the proportion of Gram-negative bacteremias have increased from 43.5% and 57.9% in mid to late 1990s to 52% and 80% respectively, in the current era. Gram-negative bacteria accounted for 46% of the bacteremias in a previous study in lung transplant recipients (1) and for 53% in ours. Notably, 57% of the Gram-negative bacteremias in our report were due to multiple antibiotic-resistant bacteria. While 35% of the patients with antibiotic resistant bacteria had cystic fibrosis compared to 8% of those with sensitive bacteria, cystic fibrosis *per se* was not significantly predictive of bacteremia due to resistant bacteria. When *B. cepacia* was excluded, the proportion of patients with cystic fibrosis and resistant Gram-negative bacteremia (50%) was virtually identical to that of patients without cystic fibrosis (48%). Overall, prior antibiotic use was the only variable significantly associated with resistant Gram-negative bacteremia.

Immunosuppression, particularly the use and type of induction regimens for lung transplant recipients has evolved considerably over the last decade (8). The use of induction therapy has increased from 22% in 1997 to 50% in 2004. Whereas antithymocyte globulin use decreased from 23% in 1995 to 5% in 2004, the use of IL-2 receptor antibody

increased from 0% in 1997 to 38% in 2004 (8). Receipt of depleting T-cell antibody was a risk factor for bacteremia in solid organ transplant recipients in one study (20), but not in another (21). Patients who were still requiring mechanical ventilation at 30 days and those receiving T-cell depleting antibody were more likely to develop bacteremia within 30 days posttransplant. Whether modification of prophylaxis or selection of therapy that is based on prior culture data or other preventive strategies can curtail this risk, remains to be determined. We caution, however, that our data are based on a small sample size and our findings therefore should be confirmed in future studies.

The only variable that significantly correlated with the risk of resistant (vs. sensitive) Gram-positive bacteremia was mycophenolate mofetil use. Mycophenolate has potent *in vitro* antifungal activity against *P. jirovecii* (22) and possesses antiviral activity against viruses such as flaviviruses (23). However, it has no known antibacterial activity or direct effects by which it may promote bacterial proliferation. The association between mycophenolate mofetil and resistance (largely due to MRSA) could not be explained on the basis of CMV infection, diabetes mellitus, neutropenia, renal failure, or prior antibiotic use and may simply be an artifactual finding based on multifactorial analyses in a small sample size.

Mortality rates in bacteremic transplant recipients have ranged from 14% in kidney, 28–36% in liver and 59% in heart transplant recipients (10,15,24). In lung transplant recipients, mortality was 22% in patients with Gram-negative and 33% in those with Gram-positive bacteremia (1). Overall mortality rate in bacteremic patients in our study was 25%. Mechanical ventilation at baseline and abnormal mental status were associated with poor outcome. The aforementioned variables while important with regards to their prognostic implications are largely unamenable once bacteremia has occurred. Discordant antibiotic use, on the other hand, is a modifiable variable. Mortality rate was 43% in patients receiving discordant antibiotics and 14% in those receiving concordant antibiotics (Table 7). Studies in critically ill patients with sepsis and with ventilator associated pneumonia have shown similar results (25,26), In the case of lung transplant recipients, the knowledge of susceptibility data of patients' preoperative or post-transplant isolates can be potentially valuable in guiding empiric antibiotic selection, particularly in those with high rate of colonization, for example, patients with cystic fibrosis or bronchiectasis.

In summary, our data show that bacteremia remains a significant complication in lung transplant recipients. Notably, 48% of the bacteremias were due to bacteria that demonstrated multiple antibiotic resistance. These data suggest that concerns regarding escalating trends in antibiotic resistance in critically ill transplant recipients must be balanced by the need for appropriate empiric antibiotic therapy. In this context, periodic evaluation of evolving trends in bacteremias has implications relevant for appropriate management and for optimal antibiotic prescription in these patients.

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